

WHAT IS CLAIMED IS:

1 1. A method for determining a methylation profile of a cell, tissue or
2 organism, the method comprising the steps of:
3 a. providing a uniform population of randomly cleaved or sheared DNA
4 from the cell or organism, wherein the DNA comprises a first portion and a second portion
5 and each portion comprises methylated and unmethylated nucleotides;
6 b. separating the second portion into a methylated DNA sub-portion and a
7 methylated DNA sub-portion;
8 c. quantifying the relative amount of at least one specific sequence in at
9 least two DNA samples selected from the group consisting of the first portion, the methylated
10 DNA sub-portion, and the unmethylated DNA sub-portion,
11 thereby determining the methylation profile of several such nucleic acid
12 sequences from a cell, tissue or organism.

1 2. The method of claim 1, wherein the method comprises the steps of:
2 labeling the at least two DNA samples with different labels, and
3 hybridizing the at least two DNA samples to a nucleic acid; and
4 determining the relative hybridization of the at least two DNA samples to the
5 specific sequence by calculating the ratio of the two hybridizing labels.

1 3. The method of claim 1, wherein the quantifying step comprises
2 quantitative amplification.

1 4. The method of claim 1, wherein the at least two DNA samples are the
2 methylated DNA sub-portion and the unmethylated DNA sub-portion.

1 5. The method of claim 1, wherein the at least two DNA samples are the
2 first portion and the methylated DNA sub-portion.

1 6. The method of claim 1, wherein the at least two DNA samples are the
2 first portion and the unmethylated DNA sub-portion.

1 7. The method of claim 1, wherein the randomly cleaved or sheared DNA
2 comprises methylated and unmethylated recognition sequences of a methyl-sensitive

3 restriction enzyme and the separating step comprises cleaving the second portion with the
4 methyl-sensitive restriction enzyme.

1 8. The method of claim 1, wherein the randomly cleaved or sheared DNA
2 comprises methylated and unmethylated recognition sequences of a methyl-dependent
3 restriction enzyme and the separating step comprises cleaving the second portion with the
4 methyl-dependent restriction enzyme.

1 9. The method of claim 2, wherein the nucleic acid is linked to a solid
2 support.

1 10. The method of claim 9, wherein the solid support is a microarray.

1 11. The method of claim 9, wherein the solid support is a bead.

1 12. The method of claim 9, wherein the solid support is a matrix.

1 13. The method of claim 1, wherein the organism is a plant.

1 14. The method of claim 1, wherein the organism is a fungus.

1 15. The method of claim 1, wherein the organism is a prokaryote.

1 16. The method of claim 15, wherein the prokaryote is a bacterial
2 pathogen.

1 17. The method of claim 16, wherein the bacterial pathogen is selected
2 from the group consisting of gram positive and gram negative species and mycobacteria..

1 18. The method of claim 1, wherein the organism is an animal.

1 19. The method of claim 18, wherein the animal is a human.

1 20. The method of claim 1, wherein the cell is a stem cell.

1 21. The method of claim 1, wherein the cell is transgenic and the nucleic
2 acid corresponds to the insertion site of a transgene.

1 22. The method of claim 1, wherein the tissue is blood.

- 1 23. The method of claim 1, wherein the tissue is biopsy tissue.
- 1 24. The method of claim 1, wherein the tissue is resected tissue.
- 1 25. The method of claim 1, wherein the tissue is normal.
- 1 26. The method of claim 1, wherein the tissue is precancerous.
- 1 27. The method of claim 1, wherein the cell is transgenic and the nucleic
2 acid corresponds to the insertion site of a transgene. In some embodiments, the tissue is
3 blood. In some embodiments, the tissue is biopsy tissue. In some embodiments, the tissue is
4 resected tissue. In some embodiments, the tissue is normal.
- 1 28. The method of claim 1, further comprising comparing the methylation
2 profile of a nucleic acid with the transcription of the nucleic acid, thereby determining the
3 relation between methylation and transcription of the nucleic acid.
- 1 29. The method of claim 28, wherein the transcription of the nucleic acid
2 is detected with a microarray.
- 1 30. The method of claim 1, further comprising comparing the methylation
2 profile of a specimen of a bacterial pathogen with a reference strain of the pathogen, wherein
3 similarity of the methylation patterns indicates common origin of the specimen and the
4 reference strain.
- 1 31. A polynucleotide microarray hybridizing to first and a second labeled
2 DNA portions, wherein the portions are from uniform populations of randomly cleaved or
3 sheared DNA from a cell or organism;
4 wherein the first DNA portion comprises unmethylated and methylated DNA
5 labeled with a first label; and
6 wherein the second DNA portion is depleted for either unmethylated DNA or
7 methylated DNA and the second portion of DNA is labeled with a second label different from
8 the first label.
- 1 32. The polynucleotide microarray of claim 31, wherein the second test
2 DNA portion is depleted for methylated DNA.

1 33. The polynucleotide microarray of claim 31, wherein the second test
2 DNA portion is depleted for unmethylated DNA.

1 34. The polynucleotide microarray of claim 31, wherein the second DNA
2 portion is depleted by
3 treating the randomly cleaved or sheared DNA with a methyl-sensitive or a
4 methyl-dependent restriction enzyme and
5 selecting uncleaved DNA.

1 35. The polynucleotide microarray of claim 31, where the DNA
2 populations are from a plant.

1 36. The polynucleotide microarray of claim 31, where the DNA
2 populations are from an animal.

1 37. The polynucleotide microarray of claim 31, where the DNA
2 populations are from a fungus.

1 38. The polynucleotide microarray of claim 31, where the DNA
2 populations are from a prokaryote.

1 39. The polynucleotide microarray of claim 38, wherein the prokaryote is a
2 bacterial pathogen.

1 40. The polynucleotide microarray of claim 39, wherein the bacterial
2 pathogen is selected from the group consisting of *Listeria*, *E. coli*, *Salmonella*, *Yersinia*, and
3 *Neisseria*.

1 41. The polynucleotide microarray of claim 31, where the DNA
2 populations are from a transgenic organism or cell.

1 42. The polynucleotide microarray of claim 31, the polynucleotide
2 microarray comprises gene promoters and/or polynucleotide sequences which when
3 methylated, silence neighboring gene expression.

1 43. A method for producing an epigenetically uniform or diverse
2 population of progeny from one or more parent individuals, the method comprising the steps
3 of:

- 4 a. determining the genomic methylation profile of sexually or asexually
5 propagated progeny of a parent individual; and
6 b. selecting progeny exhibiting a uniform or diverse methylation profile,
7 thereby producing an epigenetically uniform population from one or more parent individuals.

1 44. The method of claim 43, further comprising determining the
2 methylation profile of a parent individual and the selecting step comprises selecting progeny
3 that exhibit the methylation profile of the parent individual.

1 45. The method of claim 44, wherein the parent is an F1 hybrid.

1 46. The method of claim 43, wherein the progeny are sexually propagated.

1 47. The method of claim 43, wherein the progeny are asexually
2 propagated.

1 48. The method of claim 43, wherein the parent individual is a plant.

1 49. The method of claim 43, wherein the parent individual is an animal.

1 50. The method of claim 43, wherein the parent individual is a fungus.

1 51. The method of claim 43, wherein the parent individual is a prokaryote.

1 52. The method of claim 43, wherein the progeny are clones of the parent.

2 53. The method of claim 43, wherein the genomic methylation profile is
3 determined on a solid support.

1 54. The method of claim 53, wherein the solid support is a membrane.

1 55. The method of claim 53, wherein the solid support is a methyl binding
2 column.

1 56. The method of claim 53, wherein the solid support is a microarray.

- 1 57. The method of claim 53, wherein the solid support is a bead.
- 1 58. The method of claim 43, wherein the determining step comprises
2 separating a randomly cleaved or sheared uniform DNA population into
3 methylated and unmethylated fractions;
4 labeling the methylated or unmethylated fractions with a first label; and
5 hybridizing the methylated or unmethylated fractions to a nucleic acid.
- 1 59. The method of claim 58, wherein the method further comprises
2 providing total genomic DNA labeled with a second label and hybridizing the total genomic
3 DNA to a nucleic acid, thereby normalizing the signal from the first label.
- 1 60. The method of claim 43, wherein the randomly cleaved or sheared
2 DNA comprises methylated and unmethylated recognition sequences of a methyl-sensitive
3 restriction enzyme and the depleting step comprises cleaving the second portion with the
4 methyl-sensitive restriction enzyme.
- 1 61. The method of claim 43, wherein the randomly cleaved or sheared
2 DNA comprises methylated and unmethylated recognition sequences of a methyl-dependent
3 restriction enzyme and the depleting step comprises cleaving the second portion with the
4 methyl-dependent restriction enzyme.
- 1 62. The method of claim 43, wherein progeny are screened in groups.
- 1 63. A method of associating heterosis with methylation profiles, the
2 method comprising,
3 crossing individuals to produce progeny;
4 determining the methylation profile of the individuals and the progeny; and
5 comparing a trait of the progeny with the methylation profiles of the
6 individuals, thereby associating appearance of the trait with a methylation profile.
- 1 64. The method of claim 63, wherein the individuals are from different
2 heterotic groups.